Remarks

Claims 1-110 and 114-296 are pending. Claims 11-26, 28-35, 37-110, 143-161, and 214-287 have been allowed. Claims 111-113 have been canceled. Claims 162-213 and 288-296 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 93, 114, 129, 138 and 203 have been amended to more clearly claim what Applicants consider to be their invention.

Claims 93, 129 and 203 were amended to correct an informality. Specifically, claims 93, 129 and 203 were amended to delete the duplicated word "sample" at the end of the claims.

Claim 114 was amended to encompass all the limitations of base claim 111 from which claim 114 previously depended. Claim 114, as amended, recites a method of amplifying a target nucleic acid sequence, the method comprising bringing into contact a set of primers, DNA polymerase, and a target sample, and incubating the target sample under conditions that promote replication of the target sequence, wherein nucleic acids in the target sample are not separated from other material in the target sample, wherein replication of the target sequence results in replicated strands, wherein during replication at least one of the replicated strands is displaced from the target sequence by strand displacement replication of another replicated strand, wherein the target sample is a blood sample, a urine sample, a semen sample, a lymphatic fluid sample, a cerebrospinal fluid sample, amniotic fluid sample, a biopsy sample, a needle aspiration biopsy sample, a cancer sample, a tumor sample, a tissue sample, a cell sample, a cell lysate sample, a crude cell lysate sample, a forensic sample, an archeological sample, an infection sample, a nosocomial infection sample, a production sample, a drug preparation sample, a biological molecule production sample, a protein preparation sample, a lipid preparation sample, a carbohydrate preparation sample, or a combination thereof, or is not processed beyond cell lysis. This amendment finds support at least in original claim 111, as well as on page 3, lines 2-11; page 11, lines 5-26; page 7, line 30 through page 8, line 7; and page 43, lines 3-10.

Claim 114 was also amended to encompass all the limitations of claim 113 to recite that the target sample is not processed beyond cell lysis. This amendment finds support at least in

original claim 113, as well as on page 7, line 30 through page 8, line 7. Claims 115-136, which depend from claim 114, have not been altered.

Claim 138 was amended to recite a method of amplifying a target nucleic acid sequence using primers that are 5, 6, 7, 8, or 9 nucleotides long, wherein replication of the target sequence results in replicated strands, wherein during replication at least one of the replicated strands is displaced from the target sequence by strand displacement replication of another replicated strand. This amendment finds support at least in original claim 138 and on page 12, lines 29-31, where it is indicated that for whole genome amplification, the primers can be from 5 to 60 nucleotides long, and in particular, can be 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, and/or 20 nucleotides long.

Response to Restriction Requirement

In the Office Action mailed September 9, 2004, the claims were divided into eight groups, Group I, claims 1-161 and 214-287, drawn to methods of amplifying a target nucleic acid via strand displacement replication; Group II, claims 162-169, drawn to a method of labeling nucleic acids; Group III, claim 170, drawn to a microarray; Group IV, claims 171-182, drawn to a method of generating probes for hybridization; Group V, claims 183-210, drawn to a method of amplifying messenger RNA; Group VI, claim 211, drawn to a method of amplifying a target nucleic acid using partially degraded RNA; Group VII, claims 212-213, drawn to a method of comparative genome hybridization; and Group VIII, claims 288-296, drawn to kits.

A provisional election of the claims of Group I was made in a telephone conversation with the Examiner on August 19, 2004. As required, Applicants now affirm the election of the claims of Group I.

Objection to the Title

The title of the application was objected to on the basis that it is not descriptive of the claimed subject matter. In response, Applicants have amended the title to "MULTIPLE DISPLACEMENT AMPLIFICATION."

Objection to the Specification

The specification was objected to on the basis that inappropriate text appears on pages 23, 35 and 47. In response, Applicants have deleted the relevant paragraphs thereby removing the inappropriate text. Applicants wish to thank the Examiner for pointing out these informalities. Applicants have also amended the paragraph bridging pages 10 and 11 to correct typographical errors. Specifically, "acrude cell lysate samples" appearing on page 11, lines 15-16 was changed to "a crude cell lysate samples" and "ans/or carbohydrate" appearing on page 11, lines 18-19 was changed to "and/or carbohydrate". Applicants have also amended the paragraph bridging pages 38 and 39 to correct another informality. Specifically, an asterisk appearing on page 39, line 3, was eliminated.

Double Patenting Rejection

Claims 1-10 and 161 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,617,137. Applicants respectfully traverse this rejection.

Applicants submit with this Amendment a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c) relative to U.S. Patent No. 6,617,137. It is believed that this will obviate the present rejection pursuant to M.P.E.P. § 804.02.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 27, 36, and 111-136 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

The test for definiteness under 35 U.S.C. § 112, second paragraph is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Therefore, if one skilled in the art can understand what is encompassed by the claims, 35 U.S.C. § 112, second paragraph is satisfied.

1. Claim 27 was considered confusing in the recitation of "substantially isothermic". It is not clear why there is confusion. Isothermic conditions are generally those where the

temperature remains the same. The term substantially is used to indicate that the conditions need not be absolutely isothermic to any specific degree; the conditions merely need to be generally isothermic. Applicant submits that those of skill in the art will understand what is encompassed by this term (especially in view of well known non-isothermic techniques such as PCR). Applicant submits that this term is sufficiently definite to satisfy the requirements of 35 U.S.C. § 112, second paragraph.

2. Claim 36 was considered confusing in the recitation of "substantial complexity." It is not clear why there is confusion. Complexity is a well established term for the amount of unique sequence in a nucleic acid sample. For example, genomes typically have a complexity between 10^6 and 10^{10} base pairs. The concept of nucleic acid complexity originated in whole genome hybridization studies as a parameter to be measured and accounted for (complexity affected the rate of hybridization due to the ratio of hybridization targets to non-targets). Applicant notes that complexity has been equated to the complexity of a genomic nucleic acid sample (Page 4, lines 14-17; page 38, lines 12-15; and page 43, lines 17-20). From this, those of skill in the art would understand the meaning of the claim, thereby satisfying 35 U.S.C. § 112, second paragraph.

3. Claims 111-136 were considered confusing in the recitation of "target sample". Specifically, the Examiner alleges the claims are confusing because it cannot be determined what is encompassed by a "target sample", especially one in which nucleic acids "are not separated from other material in the target sample". Claims 111-113 have been cancelled, therefore Applicants submit the rejection under 35 U.S.C. § 112, second paragraph as it applies to claims 111-113 is moot. Applicants submit the following argument as it applies to the remaining claims 114-136 as amended.

As explained on page 11, lines 11-19 of the specification, target samples serve as a source for the target sequence, which are the object of amplification. The target sequence can be any nucleic acid and can include multiple nucleic acid molecules, such as in the case of whole genome amplification, multiple sites in a nucleic acid molecule, or a single region of a nucleic acid molecule (page 11, lines 5-8). As further described on page 11, lines 11-12, a target sequence can be in any nucleic acid sample of interest. The nucleic acid sample can be, for

example, a nucleic acid sample from one or more cells, tissue, or bodily fluids (page 11, lines 14-19). The specification further provides specific types of useful target samples containing the nucleic acid sample on page 11, lines 19-26 of the specification. These target samples are the subject matter recited in claim 114 and claimed in claims 114-136. It is well known in the art that cells, tissues and bodily fluids in such target samples contain more than just a nucleic acid component, such as proteins, lipids, etc. As such, one of skill in the art would understand that the "other material" constitutes any material present in the target sample, other than the nucleic acid. Therefore, since one of skill in the art would understand what is encompassed by a "target sample" as it is used in claims 111-136, 35 U.S.C. § 112, second paragraph is satisfied.

Rejection Under 35 U.S.C. § 102

Claims 111, 138 and 139 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,124,120 to Lizardi. Applicants respectfully traverse this rejection to the extent that it is applied to the claim as amended.

In order to anticipate claims under 35 U.S.C. § 102, it must be established that the cited art discloses each and every limitation of the claims.

Claim 111 has been canceled. Accordingly, the present rejection is moot as it applies to claim 111.

Lizardi discloses a method for amplifying nucleic acid sequences based on strand displacement replication of the nucleic acid sequences of interest by multiple primers. As described in a passage cited in the rejection (column 6, lines 22-23), the primers of Lizardi are generally 10-35 nucleotides long, but are preferably 16-24 nucleotides long. As described in a passage cited in the rejection (column 8, lines 60-63), Lizardi also discloses primers for Whole Genome Strand Displacement Amplification, where the primers have random or partially random nucleotide sequences. None of the cited passages of Lizardi specifically disclose the use of primers that are 5, 6, 7, 8, or 9 nucleotides long.

Claims 138 and 139 are drawn to a method of amplifying a target nucleic acid sequence, the method comprising, bringing into contact a set of primers, DNA polymerase, and a target sample, and incubating the target sample under conditions that promote replication of the target sequence, wherein the primers are 5, 6, 7, 8, or 9 nucleotides long, wherein replication of the target sequence results in replicated strands, wherein during replication at least one of the replicated strands is displaced from the target sequence by strand displacement replication of another replicated strand. Claim 139 is further drawn to this method wherein the set of primers comprises primers having random nucleotide sequences.

Specifically, claim 138 has been amended to require that the primers used in the claimed method be 5, 6, 7, 8, or 9 nucleotides long (this limitation is incorporated into claim 139 because claim 139 depends from claim 138). The cited passages in Lizardi fail to disclose primers of less than 10 nucleotides in length. Thus, claims 138 and 139 require a feature not specifically disclosed in the cited portions of Lizardi. Because the rejection fails to establish that Lizardi discloses every feature of the claimed method, Lizardi fails to anticipate claims 138 and 139.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $125.00, $60.00 representing the fee for a small entity under 37 C.F.R. § 1.17(a)(1) and $65.00 representing the fee for a small entity under 37 C.F.R. § 1.20(d), a Request for One Month Extension of Time, and a Terminal Disclaimer are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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Michael Laird — Date: 11/4/05